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## SEQUENCE LISTING

<110> BARBAS, Carlos F.  
RADER, Christoph

<120> HUMANIZATION OF MURINE ANTIBODY

<130> TSRI 598.0 Con.1

<140> 10/078,757

<141> 2002-02-19

<150> US 08/986,016

<151> 1997-12-05

<160> 122

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<213> Mus Musculus

<400> 27

Asp Thr Ala Met Tyr Tyr Cys Ala

1 5

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<223> Synthetic PCR Primer

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<400> 34  
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1 5

<210> 35  
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Asp Glu Ala Asp Tyr Tyr Cys  
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<210> 38  
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gaggaggagg aggaggagcc tggccggcct ggccactagt g 41

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<400> 44  
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 20 25 30  
 Trp Val Arg Gln Ile Pro Glu Lys Arg Leu Glu Trp Val Ala Lys Val  
 35 40 45  
 Ser Ser Gly Gly Gly Ser Thr Tyr Tyr Leu Asp Thr Val Gln Gly Arg  
 50 55 60  
 Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr Leu Gln Met  
 65 70 75 80  
 Ser Ser Leu Asn Ser Glu Asp Thr Ala Met Tyr Tyr Cys Ala Arg His  
 85 90 95  
 Asn Tyr Gly Ser Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val  
 100 105 110  
 Ser Ala Ala Lys Thr Thr Pro Pro Ser Val Tyr Pro Leu Ala Pro Gly  
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 Ser Ala  
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 20 25 30  
 Leu His Trp Tyr Gln Gln Lys Ser His Glu Ser Pro Arg Leu Leu Ile  
 35 40 45  
 Lys Tyr Ala Ser Gln Ser Ile Ser Gly Ile Pro Ser Arg Phe Ser Gly  
 50 55 60  
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn Ser Val Glu Thr  
 65 70 75 80  
 Glu Asp Phe Gly Met Tyr Phe Cys Gln Gln Ser Asn Ser Trp Pro His  
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 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala  
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<223> Hybrid mouse - human sequence

<400> 49  
Glu Leu Val Met Thr Gln Ser Pro Glu Phe Gln Ser Val Thr Pro Lys  
1 5 10 15  
Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Gly Thr Ser  
20 25 30  
Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile  
35 40 45  
Lys Tyr Ala Ser Gln Pro Val Phe Gly Val Pro Ser Arg Phe Arg Gly  
50 55 60  
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Tyr Ser Leu Glu Ala  
65 70 75 80  
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Asn Ser Trp Pro His  
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr  
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<210> 50

<211> 118

<212> PRT

<213> Artificial Sequence

<220>

<223> Hybrid mouse - human sequence

<400> 50

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln  
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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Ser Arg Gly  
20 25 30  
Gly Tyr Tyr Trp Ser Trp Ile Arg Gln Tyr Pro Gly Lys Gly Leu Glu  
35 40 45  
Trp Ile Gly Tyr Ile His His Ser Gly Ser Thr Tyr Tyr Asn Pro Ser  
50 55 60  
Leu Lys Ser Arg Val Thr Ile Ala Ile Asp Thr Ser Lys Asn Gln Leu  
65 70 75 80  
Ser Leu Arg Leu Thr Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr  
85 90 95  
Cys Ala Arg His Asn Tyr Gly Ser Phe Ala Tyr Trp Gly Gln Gly Thr  
100 105 110  
Leu Val Thr Val Ser Ser  
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<212> PRT

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<223> Hybrid mouse - human sequence

<400> 51

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln  
1 5 10 15  
Thr Leu Phe Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly  
20 25 30  
Gly Tyr Tyr Trp Ser Trp Ile Arg His His Pro Gly Lys Gly Leu Glu  
35 40 45  
Trp Ile Gly Tyr Ile His His Arg Ala Ala Pro Tyr Tyr Asn Pro Ser  
50 55 60  
Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Arg Asn Gln Ile  
65 70 75 80  
Ser Leu Lys Leu Arg Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr  
85 90 95  
Cys Ala Arg His Asn Tyr Gly Ser Phe Ala Tyr Trp Gly Gln Gly Thr

100 105 110  
Leu Val Thr Val Ser Ser  
115

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<220>  
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<400> 52  
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20 25 30  
Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu  
35 40 45  
Trp Ile Gly Tyr Ile His His Ser Ala Gly Thr Tyr Tyr Asn Pro Ser  
50 55 60  
Leu Lys Ser Arg Val Thr Met Ser Val Asp Thr Ser Lys Asn Gln Leu  
65 70 75 80  
Ser Leu Lys Leu Thr Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr  
85 90 95  
Cys Ala Arg His Asn Tyr Gly Ser Phe Ala Tyr Trp Gly Gln Gly Thr  
100 105 110  
Leu Val Thr Val Ser Ser  
115

<210> 53  
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<400> 53  
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu  
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Thr Leu Ser Leu Thr Cys Ser Val Ser Gly Gly Ser Ile Ser Ser Gly  
20 25 30  
Gly Tyr Tyr Trp Ser Trp Ile Arg His His Pro Gly Lys Gly Leu Glu  
35 40 45  
Trp Ile Gly Tyr Ile His His Ser Ala Gly Thr Tyr Tyr Asn Pro Ser  
50 55 60  
Leu Lys Ser Arg Val Thr Met Ser Ala Asp Thr Ser Lys Asn Gln Leu  
65 70 75 80  
Ser Leu Lys Leu Ala Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr  
85 90 95

Cys Ala Arg His Asn Tyr Gly Ser Phe Ala Tyr Trp Gly Gln Gly Thr  
100 105 110  
Leu Val Thr Val Ser Ser  
115

<210> 54  
<211> 117  
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Ser Val Arg Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Gly Phe  
20 25 30  
Ala Val Ser Trp Val Arg Gln Ala Pro Gly Gln Arg Phe Glu Trp Leu  
35 40 45  
Gly Gly Ile Val Ala Ser Leu Gly Ser Thr Asp Tyr Ala Gln Lys Phe  
50 55 60  
Gln Asp Lys Leu Thr Ile Thr Val Asp Glu Ser Thr Ala Thr Val Tyr  
65 70 75 80  
Met Glu Met Arg Asn Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys  
85 90 95  
Ala Arg His Asn Tyr Gly Ser Phe Ala Tyr Trp Gly Gln Gly Thr Leu  
100 105 110  
Val Thr Val Ser Ser  
115

<210> 55  
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<223> Hybrid mouse - human sequence

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Glu Leu Val Met Thr Gln Ser Pro Glu Phe Gln Ser Val Thr Pro Lys  
1 5 10 15  
Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Gly Asn Ser  
20 25 30  
Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile  
35 40 45  
Lys Tyr Ala Ser Gln Pro Val Phe Gly Val Pro Ser Arg Phe Arg Gly  
50 55 60  
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro  
65 70 75 80  
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Ser Asn Ser Trp Pro His

			85					90				95
Thr	Phe	Gly	Gln	Gly	Thr	Lys	Leu	Glu	Ile	Lys	Arg	Thr
			100					105				

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<400> 56  
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1 5 10 15  
Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Ala Phe Ser Ser Tyr  
20 25 30  
Asp Met Ser Trp Val Arg Gln Ile Pro Glu Lys Arg Leu Glu Trp Val  
35 40 45  
Ala Lys Val Ser Ser Gly Gly Gly Ser Thr Tyr Tyr Leu Asp Thr Val  
50 55 60  
Gln Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr  
65 70 75 80  
Leu Gln Met Ser Ser Leu Asn Ser Glu Asp Thr Ala Met Tyr Tyr Cys  
85 90 95  
Ala Arg His Asn Tyr Gly Ser Phe Ala Tyr Trp Gly Gln Gly Thr Leu  
100 105 110  
Val Thr Val Ser Ala  
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<400> 60  
Ser Ser Phe Leu Ala  
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Ser Arg Ala Thr

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Arg Ala Ser Gln Ser Ile Ser Asn  
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Lys Tyr Ala Ser Gln Ser Ile Ser  
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<210> 67  
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<400> 67  
Arg Ala Ser Gln Asp Ile Gly Thr  
1 5

<210> 68  
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<400> 68  
Lys Tyr Ala Ser Gln Pro Val Phe  
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<210> 69  
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<400> 69  
Arg Ala Ser Gln Asp Ile Gly Asn  
1 5

<210> 70  
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1 5

<210> 71  
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<400> 71  
Lys Tyr Ala Ser Gln Ser Ile Ser  
1 5

<210> 72  
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<400> 72  
Arg Ser Ser Gln Ser Ile Asn Ile  
1 5

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Tyr His Ala Ser Lys Arg Ala Ser  
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<213> Homo Sapiens

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Tyr Arg Ala Ser Ser Arg Ala Thr

1 5

<210> 76

<211> 13

<212> PRT

<213> Homo Sapiens

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Arg Ser Ser Gln Ser Leu Val Tyr Ser Asp Gly Asn Thr

1 5 10

<210> 77

<211> 8

<212> PRT

<213> Homo Sapiens

<400> 77

Tyr Lys Val Ser Asn Arg Asp Ser

1 5

<210> 78

<211> 13

<212> PRT

<213> Homo Sapiens

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Tyr Ala Ser Gln Ser Leu Val Tyr Thr Asp Gly Asn Thr

1 5 10

<210> 79

<211> 8

<212> PRT

<213> Homo Sapiens

<400> 79

Tyr Met Val Ser Asn Arg Asp Ser

1 5

<210> 80

<211> 23

<212> PRT

<213> Mus Musculus

<400> 80

Glu Leu Val Met Thr Gln Thr Pro Ala Thr Leu Ser Val Thr Pro Gly  
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Asp Ser Val Ser Leu Ser Cys  
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Glu Leu Val Met Thr Gln Ser Pro Glu Phe Gln Ser Val Thr Pro Lys  
1 5 10 15  
Glu Thr Val Thr Ile Thr Cys  
20

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<400> 82  
Arg Ala Ser Gln Ser Ile Ser Asn His Leu His  
1 5 10

<210> 83  
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<400> 83  
Arg Ala Ser Gln Asp Ile Gly Thr Ser Leu His  
1 5 10

<210> 84  
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<400> 84  
Arg Ala Ser Gln Asp Ile Gly Asn Ser Leu His  
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<210> 85  
<211> 15  
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<400> 85

Trp Tyr Gln Gln Lys Ser His Glu Ser Pro Arg Leu Leu Ile Lys  
1 5 10 15

<210> 86

<211> 15

<212> PRT

<213> Homo Sapiens

<400> 86

Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Lys  
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<212> PRT

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Tyr Ala Ser Gln Ser Ile Ser  
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<210> 88

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<212> PRT

<213> Homo Sapiens

<400> 88

Tyr Ala Ser Gln Pro Val Phe  
1 5

<210> 89

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<212> PRT

<213> Mus Musculus

<400> 89

Gly Ile Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr  
1 5 10 15  
Leu Ser Ile Asn Ser Val Glu Thr Glu Asp Phe Gly Met Tyr Phe Cys  
20 25 30

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<212> PRT

<213> Homo Sapiens

<400> 90

Gly	Val	Pro	Ser	Arg	Phe	Arg	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr
1				5					10					15	
Leu	Thr	Ile	Tyr	Ser	Leu	Glu	Ala	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys
			20					25					30		

<210> 91  
<211> 32  
<212> PRT  
<213> Homo Sapiens

Gly	Val	Pro	Ser	Arg	Phe	Arg	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr
1				5					10					15	
Leu	Thr	Ile	Ser	Arg	Leu	Glu	Pro	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys
			20					25					30		

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<212> PRT  
<213> Mus Musculus

Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys	Arg	Ala
1				5					10		

<210> 93  
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Phe	Gly	Gln	Gly	Thr	Lys	Leu	Glu	Ile	Lys	Arg	Thr
1				5					10		

<210> 94  
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<212> PRT  
<213> Mus Musculus

Glu	Val	Gln	Leu	Glu	Glu	Ser	Gly	Gly	Gly	Leu	Val	Lys	Pro	Gly	Gly
1				5					10					15	
Ser	Leu	Lys	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Ala	Phe	Ser		
			20					25					30		

<210> 95  
<211> 30  
<212> PRT

<213> Homo Sapiens

<400> 95

Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Arg	Lys	Pro	Gly	Ser
1			5						10					15	
Ser	Val	Arg	Val	Ser	Cys	Lys	Ala	Ser	Gly	Gly	Thr	Phe	Ser		
			20					25					30		

<210> 96

<211> 30

<212> PRT

<213> Homo Sapiens

<400> 96

Gln	Val	Gln	Leu	Gln	Glu	Ser	Gly	Pro	Gly	Leu	Val	Lys	Pro	Ser	Gln
1			5						10					15	
Thr	Leu	Ser	Leu	Thr	Cys	Thr	Val	Ser	Gly	Ala	Ser	Ile	Ser		
			20					25					30		

<210> 97

<211> 30

<212> PRT

<213> Homo Sapiens

<400> 97

Gln	Val	Gln	Leu	Gln	Glu	Ser	Gly	Pro	Gly	Leu	Val	Lys	Pro	Ser	Gln
1			5						10					15	
Thr	Leu	Phe	Leu	Thr	Cys	Thr	Val	Ser	Gly	Gly	Ser	Ile	Ser		
			20					25					30		

<210> 98

<211> 30

<212> PRT

<213> Homo Sapiens

<400> 98

Gln	Val	Gln	Leu	Gln	Glu	Ser	Gly	Pro	Gly	Leu	Val	Lys	Pro	Ser	Glu
1			5						10					15	
Thr	Leu	Ser	Leu	Thr	Cys	Thr	Val	Ser	Gly	Gly	Ser	Ile	Ser		
			20					25					30		

<210> 99

<211> 30

<212> PRT

<213> Homo Sapiens

<400> 99

Gln	Val	Gln	Leu	Gln	Glu	Ser	Gly	Pro	Gly	Leu	Val	Lys	Pro	Ser	Glu
1			5						10					15	

Thr Leu Ser Leu Thr Cys Ser Val Ser Gly Gly Ser Ile Ser  
20 25 30

<210> 100  
<211> 5  
<212> PRT  
<213> Mus Musculus

<400> 100  
Ser Tyr Asp Met Ser  
1 5

<210> 101  
<211> 5  
<212> PRT  
<213> Homo Sapiens

<400> 101  
Gly Phe Ala Val Ser  
1 5

<210> 102  
<211> 7  
<212> PRT  
<213> Homo Sapiens

<400> 102  
Arg Gly Gly Tyr Tyr Trp Ser  
1 5

<210> 103  
<211> 7  
<212> PRT  
<213> Homo Sapiens

<400> 103  
Ser Gly Gly Tyr Tyr Trp Ser  
1 5

<210> 104  
<211> 14  
<212> PRT  
<213> Mus Musculus

<400> 104  
Trp Val Arg Gln Ile Pro Glu Lys Arg Leu Glu Trp Val Ala  
1 5 10

<210> 105  
<211> 14  
<212> PRT  
<213> Homo Sapiens

<400> 105  
Trp Val Arg Gln Ala Pro Gly Gln Arg Phe Glu Trp Leu Gly  
1 5 10

<210> 106  
<211> 14  
<212> PRT  
<213> Homo Sapiens

<400> 106  
Trp Ile Arg Gln Tyr Pro Gly Lys Gly Leu Glu Trp Ile Gly  
1 5 10

<210> 107  
<211> 14  
<212> PRT  
<213> Homo Sapiens

<400> 107  
Trp Ile Arg His His Pro Gly Lys Gly Leu Glu Trp Ile Gly  
1 5 10

<210> 108  
<211> 14  
<212> PRT  
<213> Homo Sapiens

<400> 108  
Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu Trp Ile Gly  
1 5 10

<210> 109  
<211> 17  
<212> PRT  
<213> Homo Sapiens

<400> 109  
Gly Ile Val Ala Ser Leu Gly Ser Thr Asp Tyr Ala Gln Lys Phe Gln  
1 5 10 15  
Asp

<210> 110  
<211> 16  
<212> PRT  
<213> Homo Sapiens

<400> 110  
Tyr Ile His His Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser  
1 5 10 15

<210> 111  
<211> 16  
<212> PRT  
<213> Homo Sapiens

<400> 111  
Tyr Ile His His Arg Ala Ala Pro Tyr Tyr Asn Pro Ser Leu Lys Ser  
1 5 10 15

<210> 112  
<211> 16  
<212> PRT  
<213> Homo Sapiens

<400> 112  
Tyr Ile His His Ser Ala Gly Thr Tyr Tyr Asn Pro Ser Leu Lys Ser  
1 5 10 15

<210> 113  
<211> 32  
<212> PRT  
<213> Mus Musculus

<400> 113  
Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr Leu Gln  
1 5 10 15  
Met Ser Ser Leu Asn Ser Glu Asp Thr Ala Met Tyr Tyr Cys Ala Arg  
20 25 30

<210> 114  
<211> 32  
<212> PRT  
<213> Homo Sapiens

<400> 114  
Lys Leu Thr Ile Thr Val Asp Glu Ser Thr Ala Thr Val Tyr Met Glu  
1 5 10 15  
Met Arg Asn Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 115  
<211> 32  
<212> PRT  
<213> Homo Sapiens

<400> 115  
Arg Val Thr Ile Ala Ile Asp Thr Ser Lys Asn Gln Leu Ser Leu Arg  
1 5 10 15  
Leu Thr Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 116  
<211> 32  
<212> PRT  
<213> Homo Sapiens

<400> 116  
Arg Val Thr Ile Ser Val Asp Thr Ser Arg Asn Gln Ile Ser Leu Lys  
1 5 10 15  
Leu Arg Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 117  
<211> 32  
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<400> 117  
Arg Val Thr Met Ser Val Asp Thr Ser Lys Asn Gln Leu Ser Leu Lys  
1 5 10 15  
Leu Thr Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 118  
<211> 32  
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<213> Homo Sapiens

<400> 118  
Arg Val Thr Met Ser Ala Asp Thr Ser Lys Asn Gln Leu Ser Leu Lys  
1 5 10 15  
Leu Ala Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg  
20 25 30

<210> 119  
<211> 11  
<212> PRT  
<213> Mus Musculus

<400> 119  
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ala  
1 5 10

<210> 120  
<211> 11  
<212> PRT  
<213> Homo Sapiens

<400> 120  
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
1 5 10

<210> 121  
<211> 9  
<212> PRT  
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<221> VARIANT  
<222> (3)...(6)  
<223> Xaa = any amino acid

<400> 121  
Gln Gln Xaa Xaa Xaa Xaa Pro His Thr  
1 5

<210> 122  
<211> 8  
<212> PRT  
<213> Artificial Sequence

<220>  
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<221> VARIANT  
<222> (1)...(4)  
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<400> 122  
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1 5